REMARKS

Claims 1-57 are pending in this application, and claims 20-49 are withdrawn from consideration, as directed to non-elected subject matter in response to the November 1, 2005 requirement for restriction. Withdrawn method claims 20, 31, and 39 have been amended to incorporate the features of composition claim 1. These claims are therefore of the same scope as elected, independent claim 1 and comply with the requirements under M.P.E.P. § 821.04 for rejoinder. Applicants therefore respectfully request, upon a finding that the elected composition (preparation) claims 1-9 and 50-55 are allowable, rejoinder of withdrawn method claims 20-49.

Prior Rejections Withdrawn

Applicants appreciate the indication of the withdrawal of the prior rejections under 35 U.S.C. § 112, second paragraph.

Rejection of Claims 1-19 under 35 U.S.C. § 103

Claims 1-19 and 50-57 are rejected as obvious over Diaz-Collier *et al.*, EPO publication EP 0 559 632 A1 ("Diaz-Collier"). Applicants respectfully traverse.

The invention of the currently-rejected claims is associated with the discovery, after extensive research, of commercial-scale preparations and pharmaceutical formulations comprising TFPI or TFPI analogs which meet applicable FDA standards for purity in Phase III clinical trials (*e.g.*, less than 12% of modified species, as defined in the pending claims). These purity standards for **commercial-scale preparations** of TFPI and TFPI analogs were not achieved during attempts to scale up prior art methods, such as those described in Diaz-Collier.

Consequently, the claimed invention recites **two important features** of the TFPI and TFPI analog preparations, namely (i) commercial-grade purity (*i.e.*, less than 12% modified species) and (ii) commercial-scale quantity (*i.e.*, at least 200 grams). Applicants do not agree

that the TFPI compositions disclosed in Diaz-Collier necessarily meet the recited purity level of feature (i), for reasons already of record. However, in any event, the pending claims are **even further distinguishable** over this reference because of the recited feature (ii), namely the **quantity** of the TFPI preparation or pharmaceutical formulation.

According to Page 4 of the Office Action, "the only difference in such [claimed and prior art] preparations is the concentration of TFPI compound. One would be motivated to increase or decrease the concentration of TFPI or its derivatives ..." These assertions regarding the TFPI **concentration** are irrelevant to the claimed feature of the TFPI or TFPI analog **amount** being "at least 200 grams." That is, feature (ii) of the claimed invention discussed above is directed to the **scale or quantity** of the preparation, which is a commercial scale, and not the TFPI concentration.

Contrary what the Office Action implies on page 4, the recited feature of "at least 200 grams" is a feature of the claimed **composition**, not of a method. This feature is relevant to the claimed preparations and pharmaceutical formulations, because "**[a]ll words in a claim must be considered** in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382,1385, 165 USPQ 494, 496 (CCPA 1970) (emphasis added). Also, for a prior art reference to render a claim *prima facie* obvious, it must teach or suggest **all claim limitations**. *In re Royka*, 490 F.2d 981, 985, 180 U.S.P.Q. 580, 583 (C.C.P.A. 1974) (emphasis added). Diaz-Collier does not meet this legal standard, at least because this reference fails to suggest a TFPI composition that is on the scale of the claimed preparations or pharmaceutical formations (*i.e.*, "comprising at least 200 grams" of TFPI or TFPI analog).

In fact, the compositions disclosed in Diaz-Collier contain only "about 300 mg of highly active TFPI from a 10-liter fermentation culture." See page 345, final paragraph of Diaz-Collier,

J.A. *et al.*, THROMBOSIS AND HAEMOSTASIS, 71(3): 339-46 (1994) (already of record) [describing the same TFPI preparations as in the reference Diaz-Collier publication, EP 0 559 632 A1]. Even the "larger scale," preparation of Diaz-Collier (with only 500 mg TFPI) is **at least 400 times smaller** in protein amount than the claimed preparations or pharmaceutical formations. Nowhere does Diaz-Collier suggest a TFPI composition having a commercial quantity of at least 200 grams of protein. Nor does Diaz-Collier place the public in possession of the claimed, TFPI preparations or pharmaceutical formulations **(i) having the recited purity level and (ii) of a commercial scale**. The ability to provide the claimed, highly purified TFPI and TFPI analog preparations and pharmaceutical compositions on a large scale originates from Applicants' own disclosure, not Diaz-Collier. The need for such preparations and compositions arose from the requirements of Phase III clinical trials, which could not be satisfied during attempts to scale up prior art methods, such as those of Diaz-Collier.

The preparations and pharmaceutical formulations recited in claims 1-29 and 50-57 are therefore patentable over Diaz-Collier, whether cited under 35 U.S.C. § 102 or 35 U.S.C. § 103 of the Patent Statute. Please withdraw the rejection under 35 U.S.C. § 103.

The Rejection of Claim 19 under 35 U.S.C. § 103

Claim 19 is rejected as obvious over Diaz-Collier in view of Chen *et al.*, U.S. Patent No. 6,525,102 ("Chen"). Applicants respectfully traverse these rejections.

Claim 19 is directed to a large-scale pharmaceutical composition comprising ala-TFPI. Less than about 12% of the ala-TFPI molecules are modified species, as defined in this claim. The pharmaceutical formulation comprises 20 mM sodium citrate, 300 mM L-arginine, and 5 mM methionine, at pH 5.5. Claim 19 also recites that the pharmaceutical formulation comprises at least 200 grams of ala-TFPI.

A *prima facie* case of obviousness requires that the combined teachings of the prior art references teach or suggest all the claim limitations. *In re Royka*, 490 F.2d 981, 985, 180 U.S.P.Q. 580, 583 (C.C.P.A. 1974) (emphasis added). Diaz-Collier and Chen do not meet this standard, because combining the teachings of these references would not result in the claimed, large-scale pharmaceutical formulation. For the reasons given above, Diaz-Collier does not disclose large-scale formulations have a commercial quantity of at least 200 grams of TFPI or a TFPI analog. Chen does not remedy this deficiency of the primary reference, Diaz-Collier in arriving at Applicants' invention of claim 19.

Please withdraw this rejection under 35 U.S.C. § 103.

CONCLUSION

In view of these remarks, all pending claims of this application are believed to be in condition for allowance. Acknowledgement of the same is respectfully requested. This response is believed to completely address all of the substantive issues raised in the Office Action dated October 7, 2008.

Please continue to direct all correspondence in this application to Novartis Vaccines and Diagnostics, Inc. (formerly Chiron Corporation), Intellectual Property Dept., R440, 4560 Horton Street, Emeryville, CA 94608-2916.

Respectfully submitted,

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